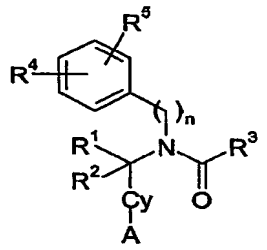
Claims

1. Use of an aryl dicarboxamide of formula (I) :



(I)

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and its racemate forms, as well as pharmaceutically acceptable salts and pharmaceutically active derivatives thereof, wherein

A is an aminocarbonyl moiety of the formula –CO-NHR^6 wherein R^6 is C_6-C_{15} alkyl, C_2-C_{15}-alkenyl, C_2-C_{15}-alkynyl, a 3-8 membered cycloalkyl, C_1-C_6 alkyl-(3-8 membered) cycloalkyl, phenyl, C_1-C_{12} alkyl phenyl, C_2-C_6-alkenyl phenyl, C_2-C_6-alkynyl phenyl;

Cy is an aryl, heteroaryl, aryl-heteroaryl, heteroaryl-aryl, aryl-aryl, cycloalkyl or heterocycle group;

n is either 0 or 1;

R^1 and R^2 are independently from each other is selected from the group consisting of hydrogen or C_1-C_6-alkyl;

R^3 is selected from the group consisting of C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkoxy, C_1-C_6-alkyl amine, C_1-C_6-alkyl alkoxy, aryl, heteroaryl, saturated or unsaturated 3-8-membered cycloalkyl, 3-8-membered heterocycloalkyl, C_1-C_6-alkyl aryl, C_1-C_6-alkyl heteroaryl, C_2-C_6-alkenyl aryl, C_2-C_6-alkenyl heteroaryl, C_2-C_6-

alkynyl aryl, C_2-C_6-alkynyl heteroaryl, C_1-C_6-alkyl cycloalkyl, C_1-C_6-alkyl heterocycloalkyl, C_2-C_6-alkenyl cycloalkyl, C_2-C_6-alkenyl heterocycloalkyl, C_2-C_6-alkynyl cycloalkyl, C_2-C_6-alkynyl heterocycloalkyl;

R^4 and R^5 are each independently from each other selected from the group consisting of H, hydroxy, C_1-C_6 alkyl, carboxy, C_1-C_6 alkoxy, C_1-C_3 alkyl carboxy, C_2-C_3 alkenyl carboxy, C_2-C_3 alkynyl carboxy, amino or R^4 and R^5 may form an unsaturated or saturated heterocyclic ring, whereby at least one of R^4 or R^5 is not a hydrogen or C_1-C_6 alkyl;

for the preparation of a medicament for the treatment and/or prevention of metabolic disorders mediated by insulin resistance or hyperglycemia, comprising diabetes, inadequate glucose tolerance, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, obesity, polycystic ovary syndrome (PCOS).

2. Use of an aryl dicarboxamide according to claim 1 for the preparation of a medicament for the treatment and/or prevention of diabetes type II, obesity or for appetite regulation.

3. Use of an aryl dicarboxamide according to claim 1 for the preparation of a pharmaceutical composition for the modulation of the activity of PTPs.

4. Use according to claim 3 wherein the PTP is PTP1B.

5. Use according to claim 4 wherein said modulation consists in the inhibition of PTP1B.

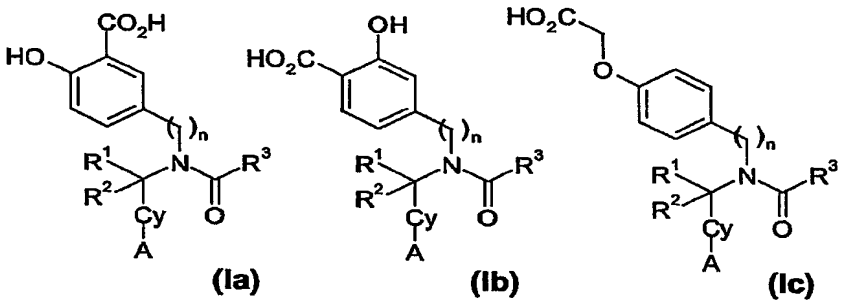
6. Use according to claim 4 for the treatment or prevention of disorders mediated by PTP1B.

7. Use according to any of claims 1 to 6, wherein R^1 and R^2 are each H.

8. Use according to any of claims 1 to 7, wherein Cy is selected from the group consisting of phenyl, thiazolyl, phenyl-thiazolyl, thiazolyl-phenyl.

9. Use according to any of claims 1 to 8, wherein A is a moiety of the formula –CO-NHR^6 wherein R^6 is C_6-C_{15} alkyl, C_2-C_{15}-alkenyl, C_2-C_{15}-alkynyl, a 3-8 membered cycloalkyl, C_1-C_6 alkyl-(3-8 membered) cycloalkyl, phenyl, C_1-C_{12} alkyl phenyl, C_2-C_6-alkenyl phenyl, C_2-C_6-alkynyl phenyl.

10. An aryl dicarboxamide according to any of the formulae (Ia), (Ib) or (Ic):



(Ia) (Ib) (Ic)

wherein

A is an aminocarbonyl moiety of the formula –CO-NHR^6 wherein R^6 is C_6-C_{15} alkyl, C_2-C_{15}-alkenyl, C_2-C_{15}-alkynyl, a 3-8 membered cycloalkyl, C_1-C_6 alkyl-(3-8 membered) cycloalkyl, phenyl, C_1-C_{12} alkyl phenyl, C_2-C_6-alkenyl phenyl, C_2-C_6-alkynyl phenyl;

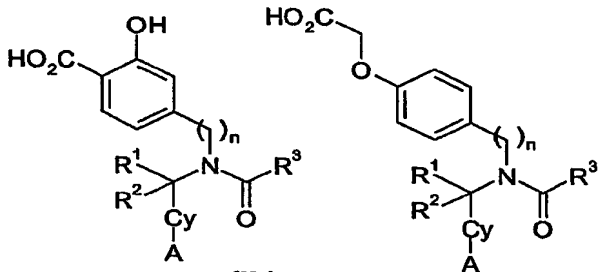
Cy is an aryl, heteroaryl, aryl-heteroaryl, heteroaryl-aryl, aryl-aryl, cycloalkyl or heterocycle group;

n is either 0 or 1;

R^1 and R^2 are independently from each other is selected from the group consisting of hydrogen or C_1-C_6-alkyl;

R^3 is selected from the group consisting of C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkoxy, C_1-C_6-alkyl amine, C_1-C_6-alkyl alkoxy, aryl, heteroaryl, saturated or unsaturated 3-8-membered cycloalkyl, 3-8-membered heterocycloalkyl, an acyl moiety, C_1-C_6-alkyl aryl, C_1-C_6-alkyl heteroaryl, C_2-C_6-alkenyl aryl, C_2-C_6-alkenyl heteroaryl, C_2-C_6-alkynyl aryl, C_2-C_6-alkynyl heteroaryl, C_1-C_6-alkyl cycloalkyl, C_1-C_6-alkyl heterocycloalkyl, C_2-C_6-alkenyl cycloalkyl, C_2-C_6-alkenyl heterocycloalkyl, C_2-C_6-alkynyl cycloalkyl, C_2-C_6-alkynyl heterocycloalkyl.

11. An aryl dicarboxamide according to formula (Ib) or (Ic):



wherein

A is an aminocarbonyl moiety of the formula –CO-NHR^6 wherein R^6 is C_6-C_{15} alkyl, C_2-C_{15}-alkenyl, C_2-C_{15}-alkynyl, a 3-8 membered cycloalkyl, C_1-C_6 alkyl-(3-8 membered) cycloalkyl, phenyl, C_1-C_{12} alkyl phenyl, C_2-C_6-alkenyl phenyl, C_2-C_6-alkynyl phenyl;

Cy is an aryl, heteroaryl, aryl-heteroaryl, heteroaryl-aryl, aryl-aryl, cycloalkyl or heterocycle group;

n is either 0 or 1;

R^1 and R^2 are independently from each other is selected from the group consisting of hydrogen or C_1-C_6-alkyl;

R^3 is selected from the group consisting of C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkoxy, C_1-C_6-alkyl amine, C_1-C_6-alkyl alkoxy, aryl, heteroaryl, saturated or unsaturated 3-8-membered cycloalkyl, 3-8-membered heterocycloalkyl, an acyl moiety, C_1-C_6-alkyl aryl, C_1-C_6-alkyl heteroaryl, C_2-C_6-alkenyl aryl, C_2-C_6-alkenyl heteroaryl, C_2-C_6-alkynyl aryl, C_2-C_6-alkynyl heteroaryl, C_1-C_6-alkyl cycloalkyl, C_1-C_6-alkyl heterocycloalkyl, C_2-C_6-alkenyl cycloalkyl, C_2-C_6-alkenyl heterocycloalkyl, C_2-C_6-alkynyl cycloalkyl, C_2-C_6-alkynyl heterocycloalkyl.

12. An aryl dicarboxamide according to claim 10 or 11, wherein R^1 and R^2 are each H.

13. An aryl dicarboxamide according to any of claims 10 to 12, wherein Cy is selected from the group consisting of phenyl, thiazolyl, phenyl-thiazolyl, thiazolyl-phenyl.

14. An aryl dicarboxamide according to claim 13, wherein R^6 is selected from the group consisting of C_8-C_{12} alkyl, C_1-C_4 alkyl phenyl which may be substituted by C_1-C_8 alkyl or phenoxy.

15. An aryl dicarboxamide according to any of the preceding claims selected from the group consisting of :

5-[(3-cyclopentylpropanoyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

5-[(3-cyclopentylpropanoyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

[4-({{[2-(4-{[(4-pentylbenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}-[(2*E*)-3-phenylprop-2-enoyl]amino}methyl)phenoxy]acetic acid

5-[(3-cyclopentylpropanoyl)(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

2-hydroxy-5-{(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)-benzoyl]amino}benzoic acid

2-hydroxy-5-[[(4-{[(4-phenoxybenzyl)amino]carbonyl}-1,3-thiazol-2-yl)methyl](3-phenylpropanoyl)amino]benzoic acid

5-{benzoyl[(4-{[(4-phenoxybenzyl)amino]carbonyl}-1,3-thiazol-2-yl)methyl]-amino}-2-hydroxybenzoic acid

2-hydroxy-5-{[(4-{[(4-phenoxybenzyl)amino]carbonyl}-1,3-thiazol-2-yl)methyl][4-(trifluoromethyl)benzoyl]amino}benzoic acid

5-[(cyclohexylcarbonyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

2-hydroxy-5-[(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)(3-phenylpropanoyl)-amino]benzoic acid

5-[benzoyl(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

5-[acetyl(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

5-[(4-cyanobenzoyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

2-hydroxy-5-[(phenoxyacetyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)-amino]-benzoic acid

2-hydroxy-5-{(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)-benzoyl]amino}benzoic acid

2-hydroxy-5-{(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)[(2*E*)-3-phenylprop-2-enoyl]amino}benzoic acid

5-[(N,N-dimethylglycyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

2-hydroxy-5-[(3-methylbut-2-enoyl)(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)-amino]benzoic acid

2-hydroxy-5-{[{4-[(octylamino)carbonyl]benzyl}(phenoxyacetyl)amino]methyl}-benzoic acid

2-hydroxy-5-({{4-[(octylamino)carbonyl]benzyl}[4-(trifluoromethyl)benzoyl]-amino}methyl)benzoic acid

2-hydroxy-5-({{4-[(octylamino)carbonyl]benzyl}[(2*E*)-3-phenylprop-2-enoyl]-amino}methyl)benzoic acid

5-{[(3-cyclopentylpropanoyl)(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)-amino]methyl}-2-hydroxybenzoic acid

2-hydroxy-5-{[(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(phenoxyacetyl)-amino]methyl}benzoic acid

2-hydroxy-5-({(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)-benzoyl]amino}methyl)benzoic acid

2-hydroxy-5-{[(3-methylbut-2-enoyl)(4-{[(4-pentylbenzyl)amino]carbonyl}-benzyl)amino]methyl}benzoic acid

5-{[(3-cyclopentylpropanoyl)(4-{[(4-phenylbutyl)amino]carbonyl}benzyl)-amino]methyl}-2-hydroxybenzoic acid

2-hydroxy-5-({[(4-{[(4-pentylbenzyl)amino]carbonyl}-1,3-thiazol-2-yl)methyl][(2*E*)-3-phenylprop-2-enoyl]amino}methyl)benzoic acid

[4-({(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)benzoyl]-amino}methyl)phenoxy]acetic acid

2-hydroxy-5-[(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(3-phenylpropanoyl)-amino]benzoic acid

4-[(3-cyclopentylpropanoyl)(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid

2-hydroxy-4-{(4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)-benzoyl]amino}benzoic acid

2-hydroxy-5-[{[2-(4-{[(4-pentylbenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}(phenoxyacetyl)amino]benzoic acid

2-hydroxy-5-{{[2-(4-{[(4-pentylbenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}[4-(trifluoromethyl)benzoyl]amino}benzoic acid

5-([(6-chloropyridin-3-yl)carbonyl]{[2-(4-{[(4-pentylbenzyl)amino]carbonyl}-phenyl)-1,3-thiazol-4-yl]methyl}amino)-2-hydroxybenzoic acid

5-((4-cyanobenzoyl){[2-(4-{[(4-pentylbenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)-2-hydroxybenzoic acid

2-hydroxy-5-((3-methylbut-2-enoyl){[2-(4-{[(4-pentylbenzyl)amino]carbonyl}-phenyl)-1,3-thiazol-4-yl]methyl}amino)benzoic acid

5-((3-cyclopentylpropanoyl){[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)-2-hydroxybenzoic acid

2-hydroxy-5-{{[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}[4-(trifluoromethyl)benzoyl]amino}benzoic acid

2-hydroxy-5-[{[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}(3-phenylpropanoyl)amino]benzoic acid

5-(benzoyl{[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)-2-hydroxybenzoic acid

[4-({{[2-(4-{[(4-pentylbenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}[4-(trifluoromethyl)benzoyl]amino}methyl)phenoxy]acetic acid

(4-{[{[2-(4-{[(4-pentylbenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}(3-phenylpropanoyl)amino]methyl}phenoxy)acetic acid

[4-({{[2-(4-{[(4-phenylbutyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}[4-(trifluoromethyl)benzoyl]amino}methyl)phenoxy]acetic acid

(4-{[{[2-(4-{[(4-phenylbutyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}(3-phenylpropanoyl)amino]methyl}phenoxy)acetic acid

[4-({{[2-(4-{[(4-phenylbutyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}[(2*E*)-3-phenylprop-2-enoyl]amino}methyl)phenoxy]acetic acid

{4-[((N,N-dimethylglycyl){[2-(4-{[(4-phenylbutyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)methyl]phenoxy}acetic acid

{4-[((cyclohexylcarbonyl){[2-(4-{[(4-phenylbutyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)methyl]phenoxy}acetic acid

{4-[((phenoxyacetyl){[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)methyl]phenoxy}acetic acid

[4-({{[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}[4-(trifluoromethyl)benzoyl]amino}methyl)phenoxy]acetic acid

(4-{[{[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}(3-phenylpropanoyl)amino]methyl}phenoxy)acetic acid

{4-[((cyclohexylcarbonyl){[2-(4-{[(4-phenoxybenzyl)amino]carbonyl}phenyl)-1,3-thiazol-4-yl]methyl}amino)methyl]phenoxy}acetic acid

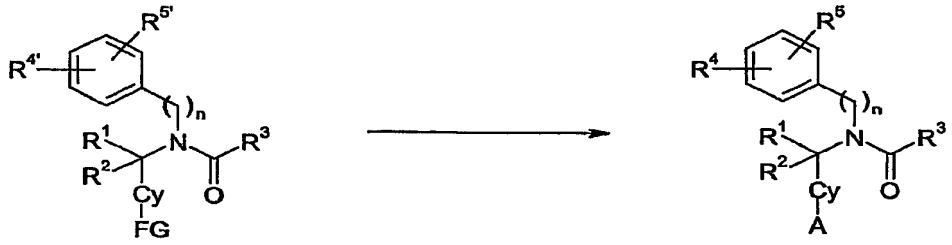
[4-({[(2-{4-[(octylamino)carbonyl]phenyl}-1,3-thiazol-4-yl)methyl][4-(trifluoromethyl)benzoyl]amino}methyl)phenoxy]acetic acid

(4-{[[(2-{4-[(octylamino)carbonyl]phenyl}-1,3-thiazol-4-yl)methyl](3-phenylpropanoyl)amino]methyl}phenoxy)acetic acid

16. An aryl dicarboxamide according to any of the claims 10 to 15 for use as a medicament.

17. A pharmaceutical composition containing at least one aryl dicarboxamide according to any of claims 10 to 15 and a pharmaceutically acceptable carrier, diluent or excipient thereof.

18. A method of preparing an aryl dicarboxamide according to any of claims 10 to 15, comprising the de-protection and/or tansformation step of :



(I') (I)

wherein R^1, R^2, R^3, R^4, R^5, $R^{4'}$, $R^{5'}$, n and Cy are as above defined and FG is A or a leaving group.